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No. 84-1032

In the Supreme Court of the United States

OCTOBER TERM, 1984

ALCON LABORATORIES, INC., ET AL., PETITIONERS

v.

UNITED STATES OF AMERICA

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FIRST CIRCUIT

BRIEF FOR THE UNITED STATES IN OPPOSITION

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QUESTION PRESENTED

Whether the court of appeals correctly concluded that petitioners' prescription drug product was an unapproved new drug that could not legally be sold without premarketing approval by the Food and Drug Administration.

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OPINIONS BELOW

The opinion of the court of appeals (Pet. App. 1a-28a) is reported at 745 F.2d 105. A prior opinion of the court of appeals (Pet. App. 49a-74a) is reported at 636 F.2d 876, cert. denied, 451 U.S. 1017. The district court order denying the government's motion for judgment notwithstanding the verdict (Pet. App. 30a-37a) is unreported. A prior opinion of the district court (Pet. App. 42a-48a) is unreported.

JURISDICTION

The judgment of the court of appeals (Pet. App. 29a) was entered on September 28, 1984. The petition for a writ of certiorari was filed on December 27, 1984. The jurisdiction of this Court is invoked under 28 U.S.C. 1254(1).

STATEMENT

1. This case concerns the regulation of "new drugs" under the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 301 *et seq.* Specifically at issue is the status of WANS, a prescription antiemetic (anti-vomiting) drug manufactured by Alcon Laboratories (Puerto Rico), Inc. The drug's active ingredients are pyrilamine maleate (an antihistamine) and pento-barbital sodium (a barbiturate). The Food and Drug Administration (FDA) has never approved the marketing of these ingredients or any similar combination drug for the treatment of nausea and vomiting (Pet. App. 5a-6a).

The court of appeals held that WANS products are "new drugs" within the meaning of the Act and therefore require premarketing approval by the FDA. In so holding, the court also rejected petitioners' contention that WANS is exempt from the new drug approval requirements under the Act's grandfather provisions.

2. Section 505(a) of the Act, 21 U.S.C. 355(a), prohibits any person from introducing into interstate commerce any "new drug" that has not been approved by FDA. The term "new drug" is defined in Section 201(p), 21 U.S.C. 321(p), as any drug that "is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof,"[1] or that has not been used to a material extent and for a material time under other than experimental conditions.

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[1]A drug can be "generally recognized" within the meaning of the Act only when there is an expert consensus founded upon the type of scientific evidence necessary for premarket approval of a new drug application. *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 632 (1973).

The requirement that a drug be "effective" to escape new drug status was added to the Act in 1962. Pub. L. No. 87-781, § 102, 76 Stat. 781. Prior to that time a drug needed to meet only the standards for establishing "safety." The 1962 amendments accommodated the need for a transition to the new regulatory scheme by excluding from the "new drug" approval requirements certain drugs that were available in the domestic market prior to 1962. The grandfather clause, Pub. L. No. 87-781, § 107(c)(4), 76 Stat. 789, applies if a manufacturer can establish, inter alia, that the conditions of use, as indicated on the product's labeling, have not changed since 1962 and that the drug was generally recognized as safe prior to the enactment date of the amendments.[2] If the product meets the statutory standards, it need not satisfy the "effectiveness" requirement added to the Act in 1962. Of course, the product must satisfy the requirement that the drug be generally recognized by experts as safe. See *United States* v. *Western Serum Co.*, 666 F.2d 335, 339-341 (9th Cir. 1982).

3. The drugs involved in this case were first marketed in 1955 and 1956 and have never been approved for safety and effectiveness by FDA. In 1978, the government initiated seizure and injunction proceedings against WANS products and their current manufacturer, charging that the products were unapproved new drugs that could not legally

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[2]The relevant grandfather clause, Pub. L. No. 87-781, § 107(c)(4), 76 Stat. 789, provides that:

> In the case of any drug which, on the day immediately preceding the enactment date [*i.e.*, October 9, 1962], (A) was commercially used or sold in the United States, (B) was not a new drug as defined by section 201(p) of the basic Act as then in force, and (C) was not covered by an effective application under section 505 of that Act, the amendments to section 201(p) made by this Act shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day.

be marketed.[3] In response, petitioners contended that WANS products were not subject to the Act's new drug approval requirements for two reasons: first, because they were exempt under the 1962 grandfather provisions; and, second, because they were now generally recognized as safe and effective (Pet. App. 9a).

At trial, the jury answered special interrogatories indicating that WANS qualified for the grandfather clause exemption and, further, that the products were today generally recognized by experts as safe and effective (Pet. App. 76a) and thus were not a "new drug" at all. The district court denied the government's motions for a directed verdict and for judgment notwithstanding the verdict (*id.* at 42a-48a).

4. The court of appeals reversed (Pet. App. 1a-28a). In an opinion written by Justice Stewart, sitting by designation, the panel unanimously held that the government's motion for a directed verdict should have been granted.

The court of appeals rejected petitioners' claim to the grandfather clause exemption for two reasons. First, the conditions of use recited in their labeling had changed since 1962 (Pet. App. 18a-20a) and, second, there was no evidence whatever that, in 1962, the products were generally recognized as safe by qualified experts (*id.* at 22a, 27a). Petitioners had produced no evidence of scientific testing upon which a finding of general recognition of safety could be based (*ibid.*).

The court of appeals also rejected petitioners' contention that, even if the grandfather clause did not apply, premarketing approval was not required because WANS products

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[3]After drug products containing the same active ingredients as WANS came to FDA's attention, all manufacturers of such products — except petitioner Alcon — voluntarily removed them from the market.

were now generally recognized as safe and effective by qualified experts. The court found petitioners' evidence on this issue to be fatally defective because, among other reasons, one of petitioners' experts testified that the studies upon which petitioners relied were not adequate and well-controlled by today's standards (Pet. App. 26a-27a).

In addition, the court of appeals noted (Pet. App. 24a-27a) that the three studies upon which petitioners relied did not even involve WANS products. Instead, the studies tested Emeserts, a drug that had been withdrawn from the market by its manufacturer. It was undisputed that the effectiveness of WANS products themselves had never been tested. Moreover, petitioners introduced no evidence of bioequivalency testing to show that results of the studies on Emeserts would apply to WANS (*id.* at 25a).[4] See *United States* v. *Generix Drug Corp.*, 460 U.S. 453, 455 (1983). Even petitioners' expert witness did not testify that the tested products were bioequivalent to WANS; he stated only that the drugs were identical "or nearly so" (Pet. App. 25a). The court of appeals therefore concluded that the absence of any expert testimony about inactive ingredients precluded a finding of bioequivalence as a matter of law (*ibid.*).[5]

ARGUMENT

1. Petitioners' principal quarrel appears to be with the manner in which the court of appeals applied settled principles to the particular facts of this case. Petitioners contend (Pet. 9) that the court of appeals held that "a change in labeling which adds additional warnings and precautions

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[4]Emeserts had the same active ingredients as WANS, but the record does not reveal its inactive ingredients (Pet. App. 24a).

[5]On November 1, 1984, Justice Brennan denied petitioners' motion to stay the court of appeals' mandate. No. A-334.

automatically takes the product out of 'grandfather' status." This, petitioners submit, is contrary to public policy and would discourage manufacturers from revising labels to provide additional consumer information or to delete unwarranted claims (*ibid.*).

Petitioners' argument misreads the court of appeals' opinion. In fact, the court expressly stated (Pet. App. 18a) that it was not reaching the question whether corrective labeling alone would transform a product into a "new drug" and trigger FDA approval requirements. Rather, the court rejected petitioners' claim to the grandfather exemption for two independent reasons. First, after a detailed comparison of WANS' labeling in 1962 and at present, the court concluded that the current label suggests use for conditions that were not listed in 1962. *Ibid.* See also *United States* v. *Allan Drug Corp.*, 357 F.2d 713 (10th Cir.), cert. denied, 385 U.S. 899 (1966); *United States* v. *1,048,000 Capsules*, 347 F. Supp. 768 (S.D. Tex. 1972), aff'd, 494 F.2d 1158 (5th Cir. 1974). In addition, the court relied on the undisputed lack of pre-1962 scientific testing of WANS (Pet. App. 19a) to reject petitioners' claim of grandfather status: "[e]ven if WANS met the labeling condition of the grandfather clause, the clause would still be inapplicable as a matter of law * * *."

2. There is no merit to petitioners' contention (Pet. 16-17) that the court of appeals misapplied the teachings of *Weinberger* v. *Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609 (1973), and *Weinberger* v. *Bentex Pharmaceuticals, Inc.*, 412 U.S. 645 (1973), in requiring that at least some scientific drug testing for safety must have been performed prior to 1962 to fulfill the general recognition requirement of the grandfather clause. In fact, petitioners argue merely that *Hynson* is not controlling because it involved only the evidentiary requirements of the 1962 amendments for demonstrating effectiveness, and not

those for safety. The court of appeals recognized that distinction (Pet. App. 21a n.17), but correctly concluded that it provided "no justification for ignoring the Court's reasoning." Thus, the rationale this Court stated in *Hynson* has been faithfully applied; the decision below does not, as petitioners suggest, conflict with *Hynson*. See also *United States* v. *41 Cases, More or Less,* 420 F.2d 1126, 1130 (5th Cir. 1970) (the absence of literature establishing *safety* is proof that a product is not generally recognized as safe); *United States* v. *Articles of Drug Labeled Colchicine,* 442 F. Supp. 1236, 1243 (S.D.N.Y. 1978), aff'd, 603 F.2d 215 (2d Cir. 1979) (grandfather status denied due to absence of published literature to support general recognition of safety in 1962).

3. The court below reviewed the evidence and, on the basis of established precedent, found that petitioners' products were not exempt from the statutory premarketing approval procedures. See, *e.g., United States* v. *Western Serum Co.,* 666 F.2d 335 (9th Cir. 1982); *Premo Pharmaceutical Laboratories, Inc.* v. *United States,* 629 F.2d 795 (2d Cir. 1980); *United States* v. *Articles of Drug . . . Hormonin,* 498 F. Supp. 424 (D.N.J. 1980), aff'd mem., 672 F.2d 904 (3d Cir. 1981). Contrary to petitioners' suggestion (Pet. 26), the court did not ignore the testimony of one of petitioners' experts concerning the alleged bioequivalence of WANS and Emeserts. The court found instead that the testimony was insufficient, as a matter of law, to prove that WANS and Emeserts — a product that had been pulled from the market — were bioequivalent (Pet. App. 25a). For that reason, as the court of appeals observed (*id.* at 25a n.20), the case does not raise any issues left unresolved by

this Court in *United States* v. *Generix Drug Corp.*, 460 U.S. at 461.[6]

4. Petitioners' remaining contentions are equally without merit. The court of appeals did not conclude that "it will be left to the courts, rather than qualified experts, to determine whether clinical trials reported in the published literature are 'adequate and well controlled' " (Pet. 22 (emphasis deleted)). Nor did the court below "reach[] well beyond its own guidelines for judicial review" (*id.* at 23-24). Rather, the court found only that the record in this case did not present a genuine issue of material fact (Pet. App. 23a-26a).

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[6]The respondents in *Generix* contended that they did not have to obtain FDA approval for their copy of a legally-marketed drug. Because there was no showing of bioequivalence, this Court did not reach the question whether "two demonstrably bioequivalent products * * * might under some circumstances be the same 'drug.' " 460 U.S. at 461. The issue need not be reached here for the same reason; as the court of appeals noted, bioequivalence was not demonstrated. In any event, even if petitioners had successfully proved bioequivalence, this case would still not present the question left open in *Generix*. All petitioners would have established is that WANS was functionally identical to an unapproved new drug, a product that cannot legally be sold.

CONCLUSION

The petition for a writ of certiorari should be denied.

Respectfully submitted.

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